

Bringing Artificial Intelligence into Diagnostics and  
Clinical Practice

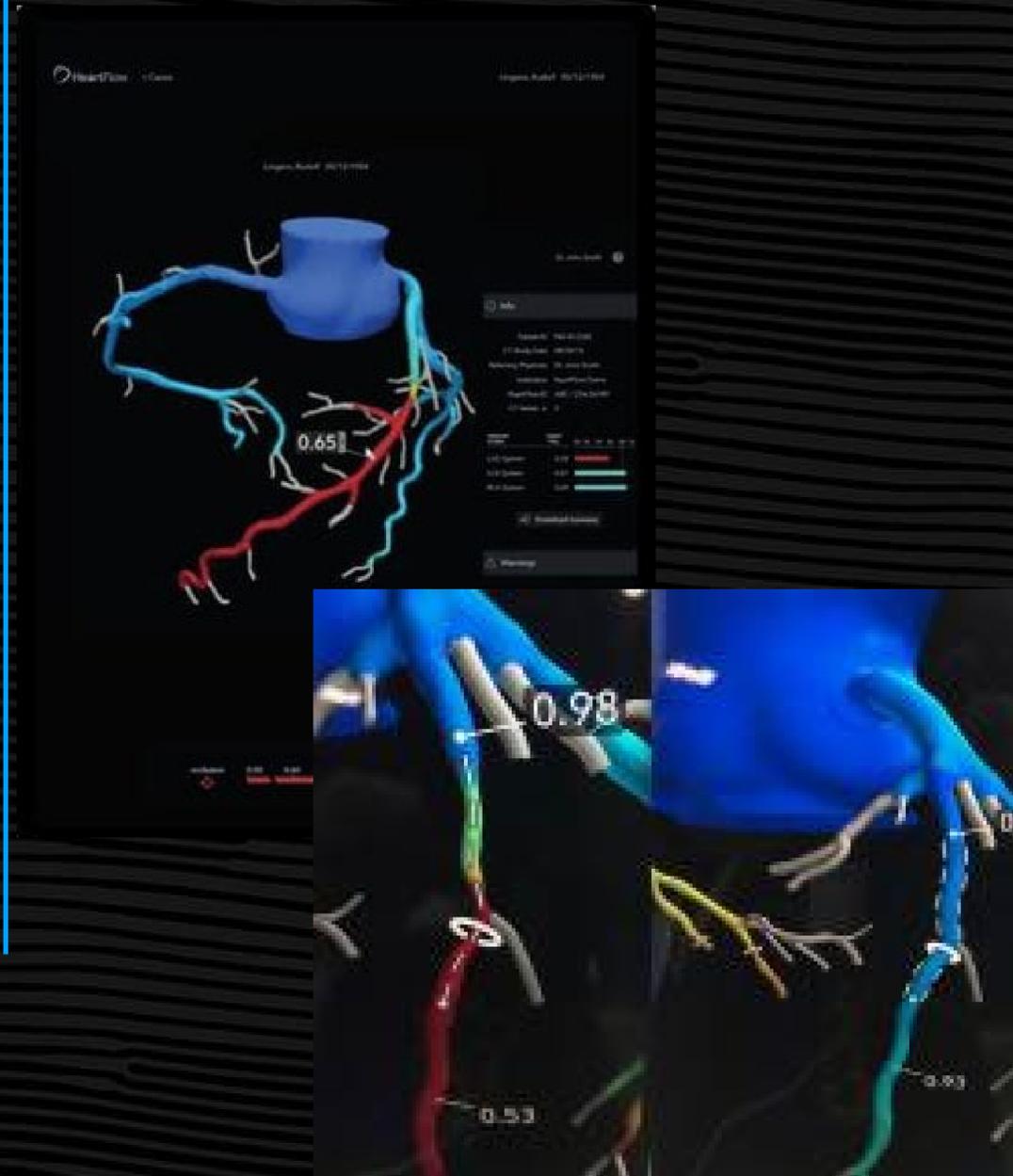
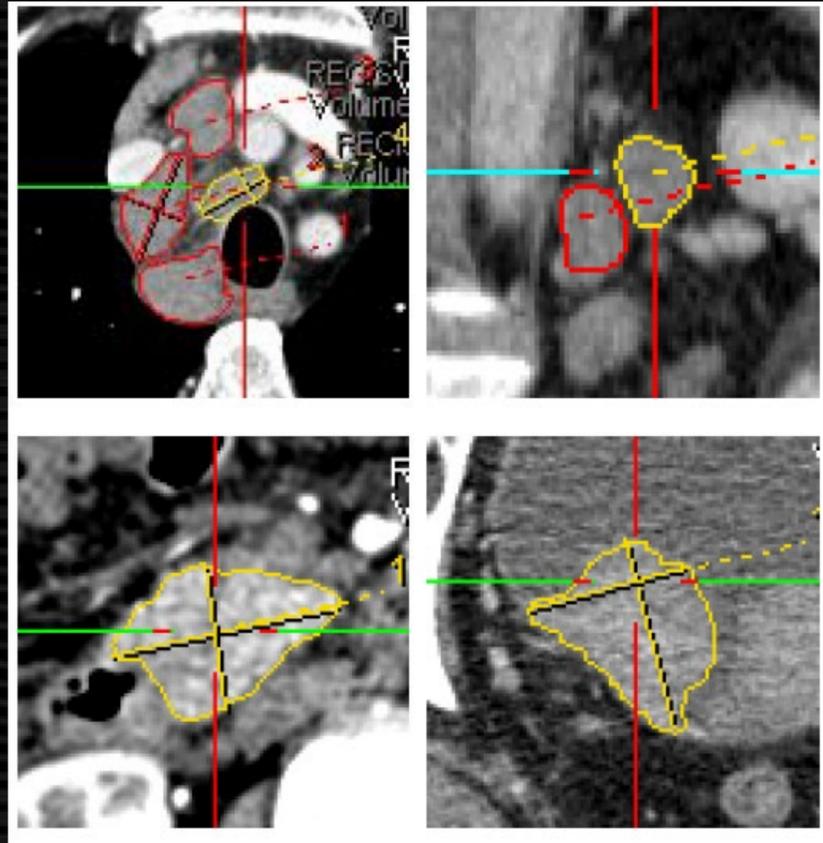


**JONA**

Leo Grady, PhD

Founder and CEO of Jona

JONA PhD in artificial intelligence 20 years ago





# Getting paid for AI

## Why focus on getting paid for AI

The world wants medical AI to be:

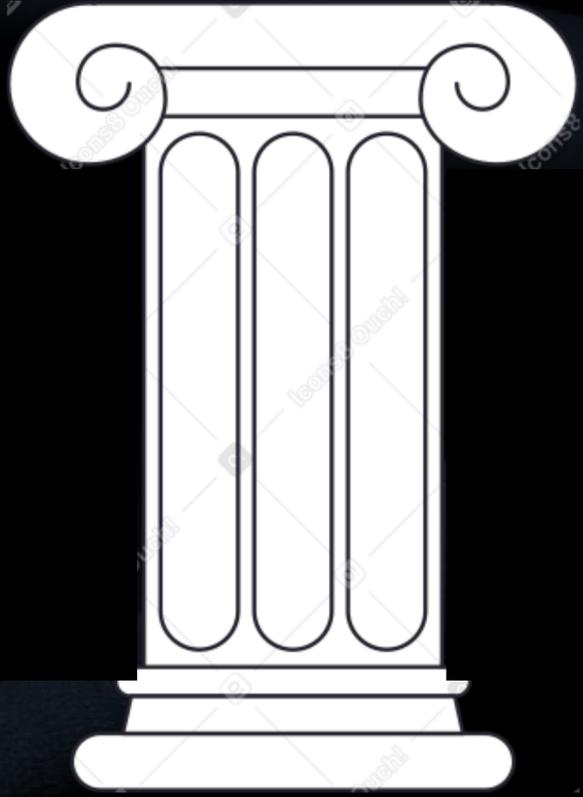
- Robust
- Unbiased
- Dependable
- Clinically validated

*Requires serious financial investment to develop this technology and so there must be financial return*

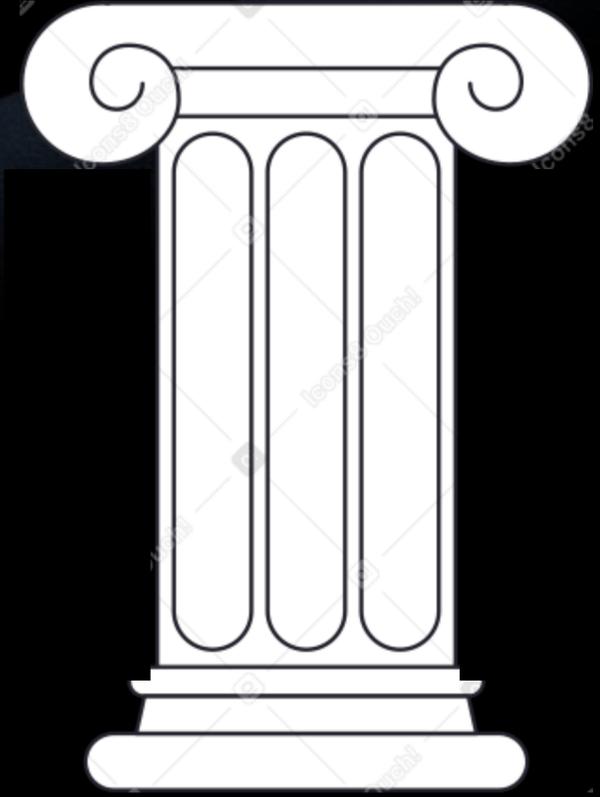


# Getting paid for AI

Two pillars



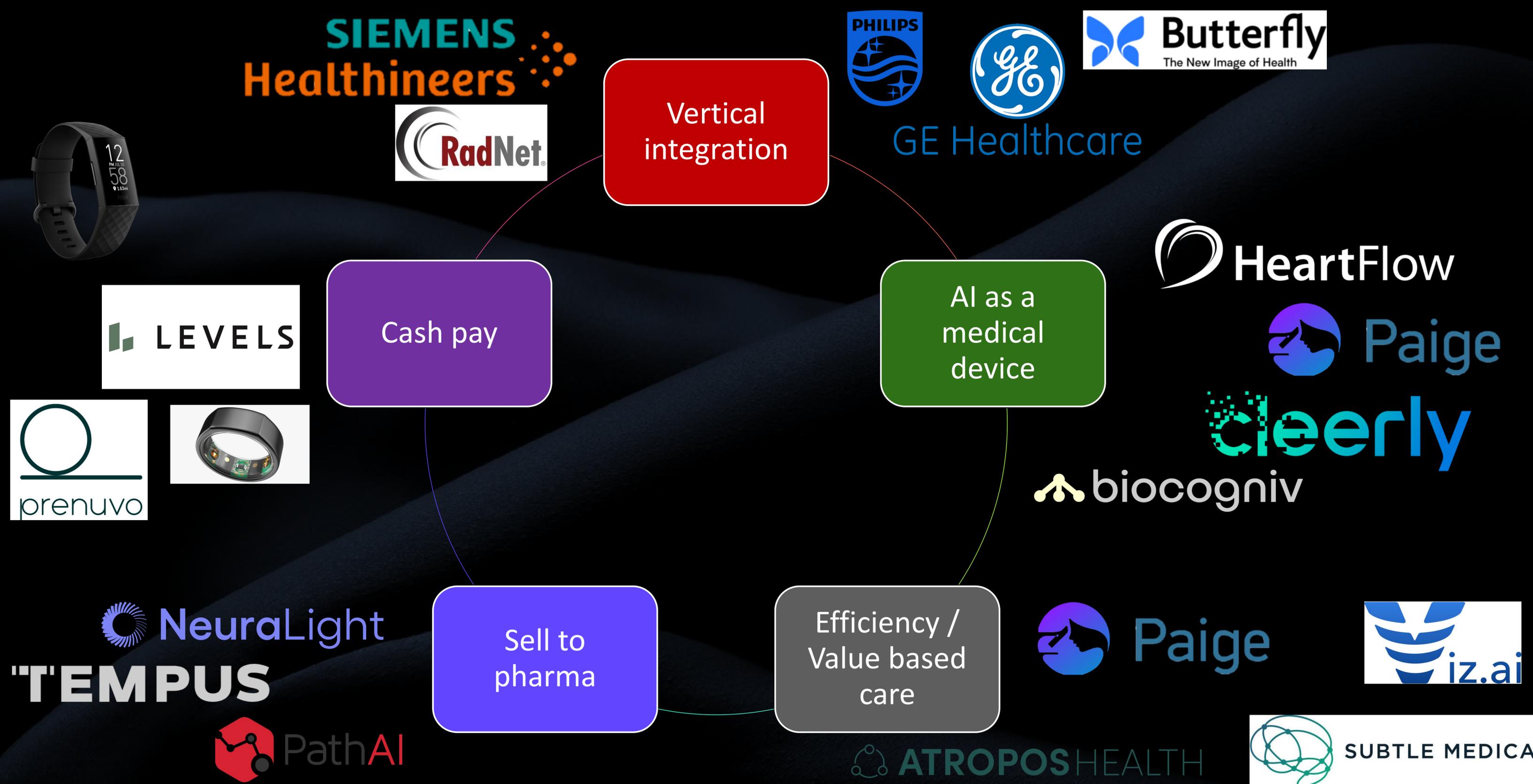
*Business model*



*Perception of value*



# Five business models for AI in healthcare





# Perception of value

Perceived value > Cost **BUY**

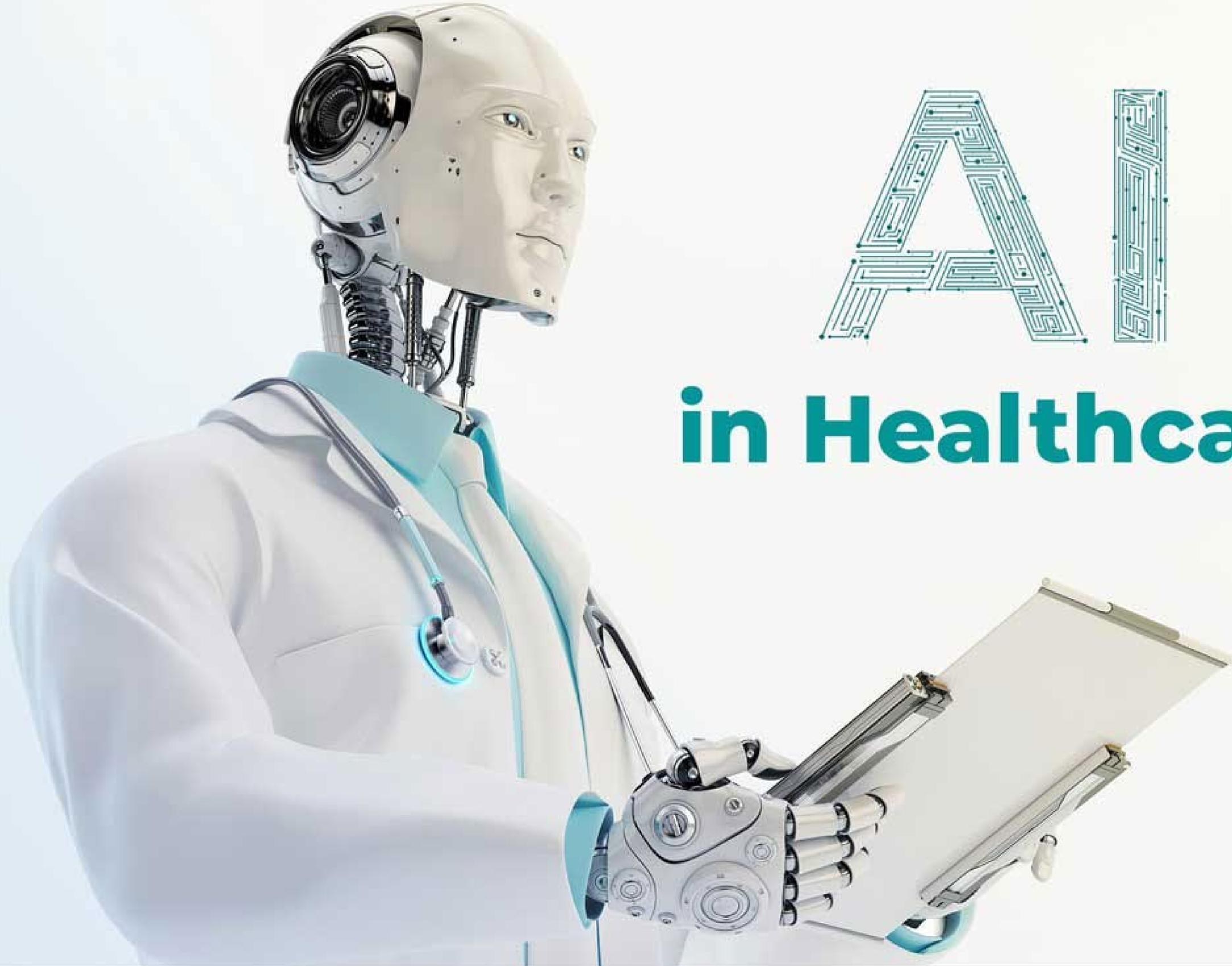
Perceived value < Cost **PASS**

*Buy also means “adopt”*

## Perceived Value - Many factors

- Actual value (data and proof)
  - Scarcity, urgency, FOMO
  - Company brand
  - Testimonial from trusted customers
  - Price
- 
- **Comparators**
    - What is the value of *similar* products/technologies?

*What is similar to AI?*



AI

**in Healthcare**

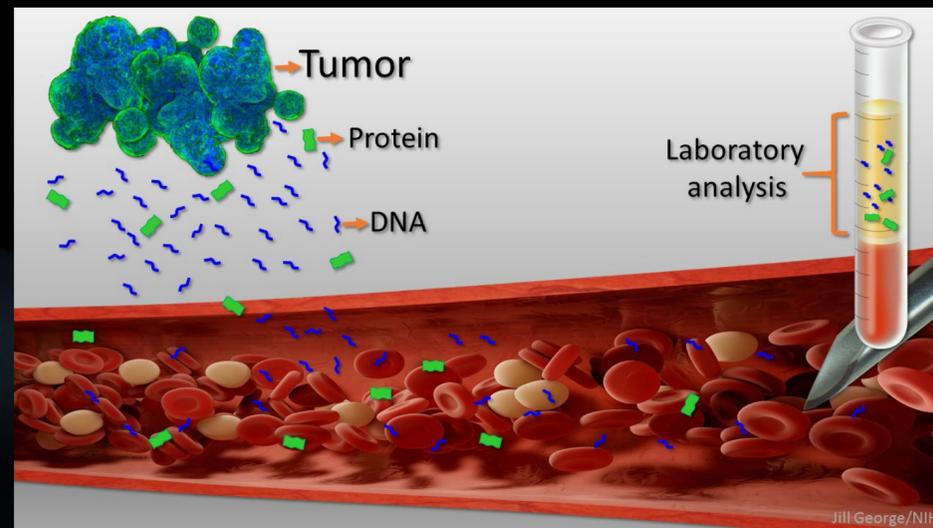


# Clinical comparators

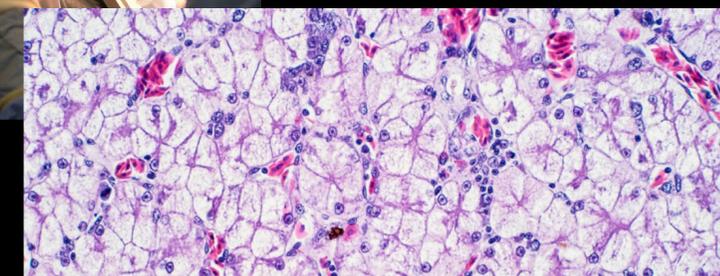
## Blood test



Liquid Biopsy  
GRAIL price: \$950



## Biopsy



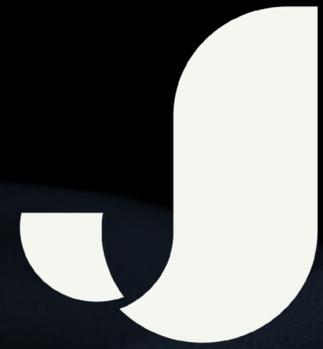
← Is it? →

### Low value

- LabCorp schedule fee for 2024:
- Women's health blood test: \$199
- Men's health blood test: \$199
- General health blood test: \$99
- Comprehensive wellness blood test: \$169
- Vitamin deficiency blood test: \$159
- Anemia blood test: \$179
- Liver health blood test: \$59
- PSA prostate cancer screening test: \$69

### High value

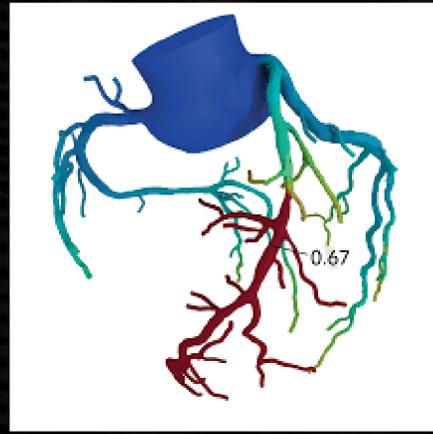
- High skill procedures
- Average USA costs of biopsy by different tumor type:
  - Prostate: \$2,020
  - Skin: \$575
  - Breast: \$3,000
  - Liver: \$4,500
  - Kidney: \$6,500



JONA

# JONA

## Cardiovascular CT



High value AI extraction and interpretation

## Pathology



## Microbiome



### Organisms

We identified 3 organisms that are associated with Constipation

- LOW Bifidobacterium
- HIGH Bacteroides
- NORMAL Butyricicoccus

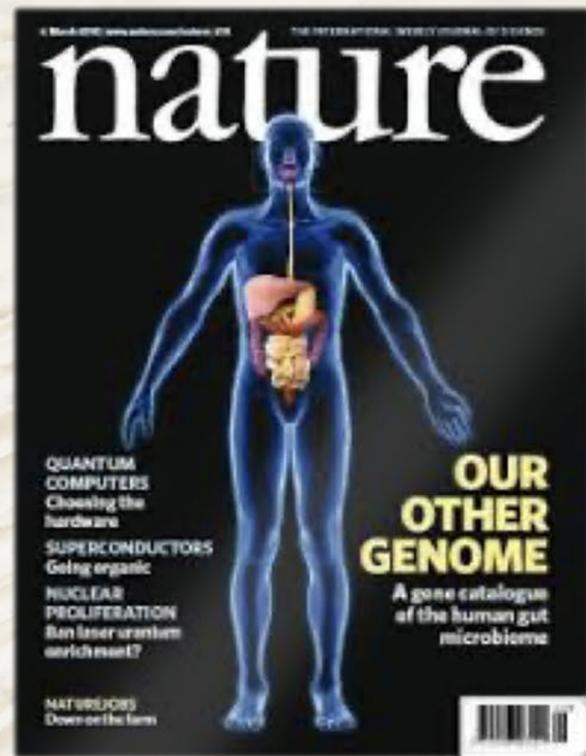
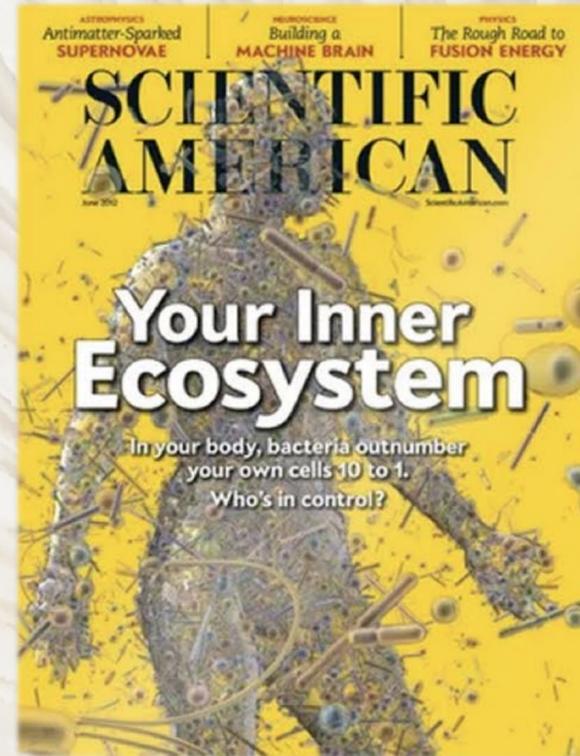
## Hardware/lab



Technical component  
Professional component  
and  
Digitization

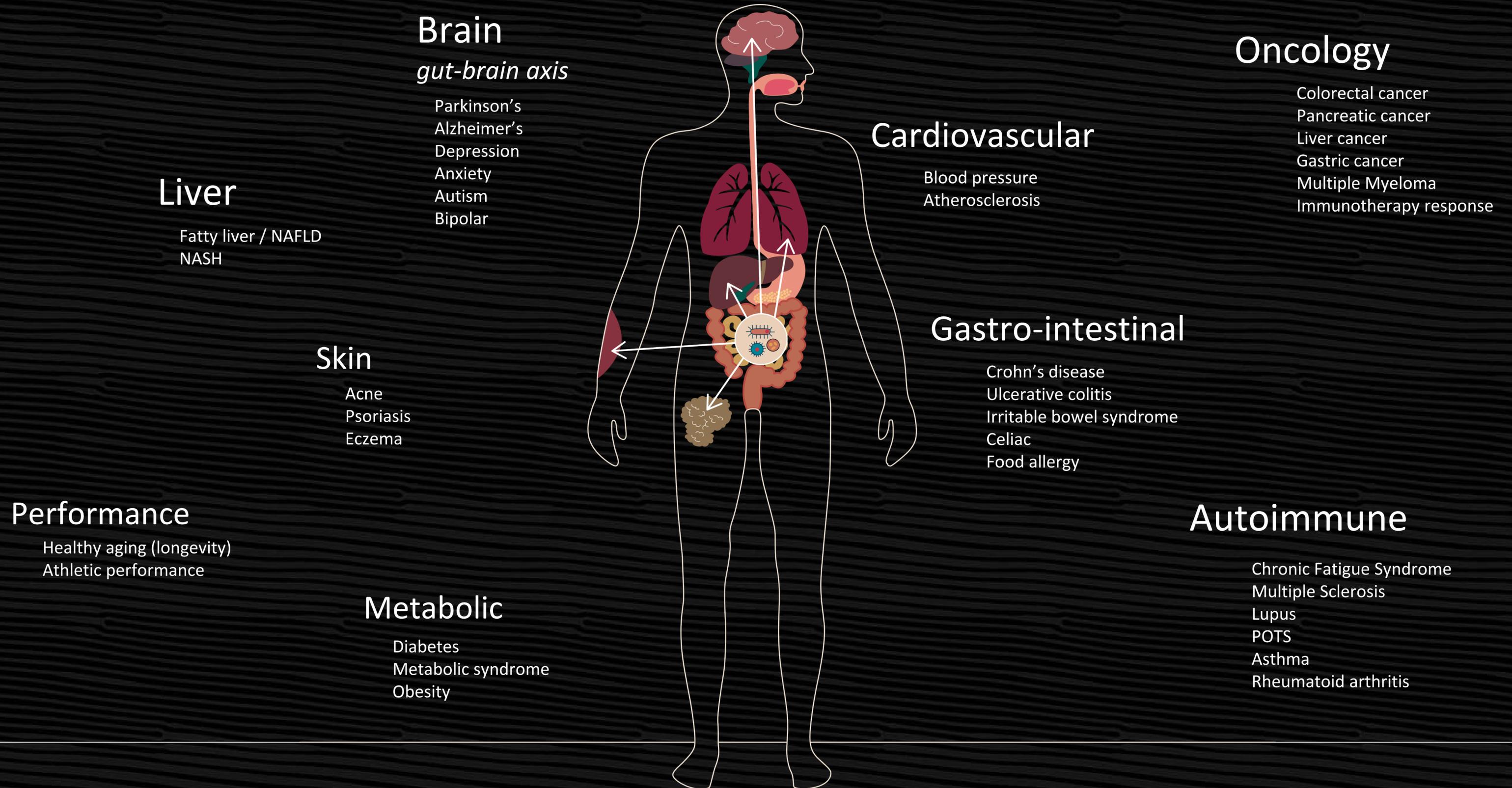


JONA

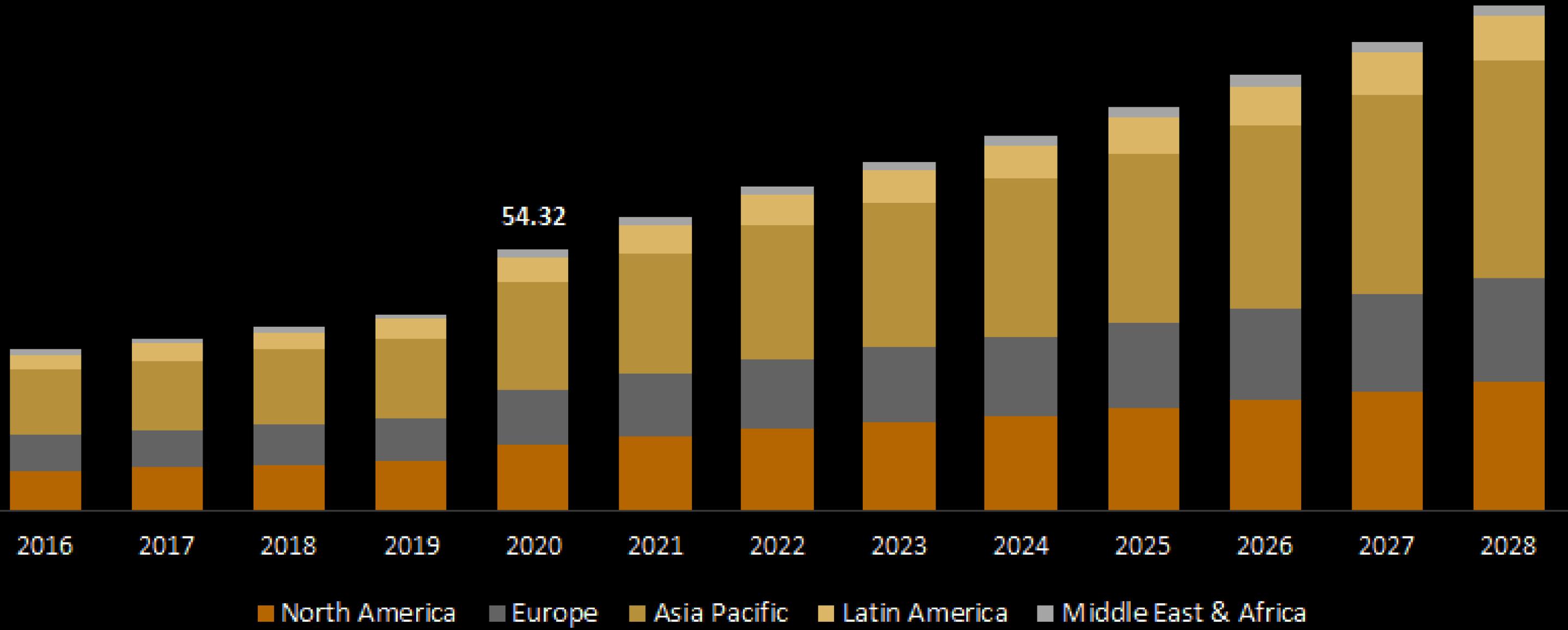




The gut microbiome has been linked to nearly every system and health condition in the body



Probiotics Market Size, By Region, 2016 - 2028  
(USD Billion)



Source: Polaris Market Research Analysis



Pathogens		
<b>Bacterial Pathogens</b>		
	Result	Normal
<i>Campylobacter</i>	<dl	<1.00e3
<i>C. difficile</i> , Toxin A	<dl	<1.00e3
<i>C. difficile</i> , Toxin B	<dl	<1.00e3
Enterohemorrhagic <i>E. coli</i>	<dl	<1.00e3
<i>E. coli</i> O157	<dl	<1.00e3
Enteroinvasive <i>E. coli</i> /Shigella	<dl	<1.00e2
Enterotoxigenic <i>E. coli</i> LT/ST	<dl	<1.00e3
Shiga-like Toxin <i>E. coli</i> stx1	<dl	<1.00e3
Shiga-like Toxin <i>E. coli</i> stx2	<dl	<1.00e3
<i>Salmonella</i>	<dl	<1.00e4
<i>Vibrio cholerae</i>	<dl	<1.00e5
<i>Yersinia enterocolitica</i>	<dl	<1.00e5
<b>Parasitic Pathogens</b>		
	Result	Normal
<i>Cryptosporidium</i>	<dl	<1.00e6
<i>Entamoeba histolytica</i>	<dl	<1.00e4
<i>Giardia</i>	<dl	<5.00e3
<b>Viral Pathogens</b>		
	Result	Normal
Adenovirus 40/41	<dl	<1.00e10
Norovirus GI/II	<dl	<1.00e7
Normal Bacterial Flora		
	Result	Normal
<i>Bacteroides fragilis</i>	9.56e10	1.60e9 - 2.50e11
<i>Bifidobacterium</i> spp.	7.07e10	>6.70e7
<i>Enterococcus</i> spp.	4.69e5	1.9e5 - 2.00e8
<i>Escherichia</i> spp.	4.54e6	3.70e6 - 3.80e9
<i>Lactobacillus</i> spp.	4.96e8	8.6e5 - 6.20e8
Clostridia (class)	9.96e6	5.00e6 - 5.00e7
<i>Enterobacter</i> spp.	2.22e6	1.00e6 - 5.00e7
<i>Akkermansia muciniphila</i>	<dl	1.00e1 - 5.00e4
<i>Faecalibacterium prausnitzii</i>	1.07e6	1.00e3 - 5.00e8

PCR panel

Fixed number of organisms

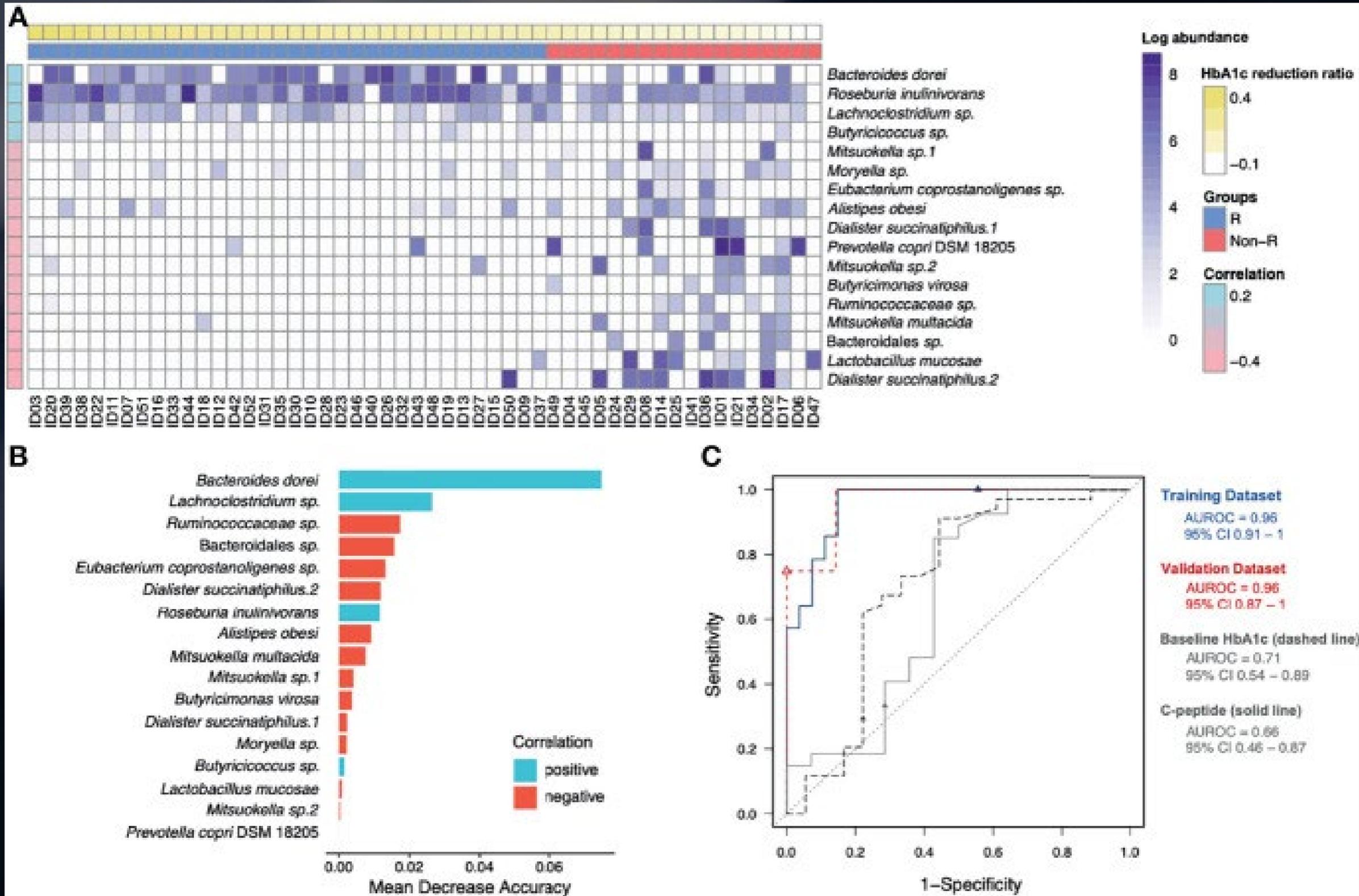
Information too limited, no analysis or actionability (except antibiotics)



Cohort	Microbiota Findings
Obese cohort [10, 11, 22, 29–32]	↓ <i>Rikenellaceae</i> and <i>Christensenellaceae</i> ↓ <i>Bifidobacterium</i> , <i>Oscillospira</i> and <i>Akkermansia</i>
Obese cohort [33]	↓ <i>Alistipes finegoldii</i> and <i>Alistipes senegalensis</i>
Obese cohort [34]	<i>Alistipes</i> = marker of persistent weight loss success
Obese cohort [11, 35]	↓ <i>Faecali prausnitzii</i>
Obese cohort [21, 32, 36]	Weight loss ↑ <i>Faecali prausnitzii</i> , <i>Akkermansia</i> and <i>Christensenellaceae</i>
Obese cohort [37]	↑ Prevotellaceae, Coriobacteriaceae, Erysipelotrichaceae, and Alcaligenaceae
Elevated BMI [38, 39]	↑ <i>Roseburia</i>
Obese cohort [40]	↑ <i>Eubacterium dolichum</i>
Obese cohort [37]	↑ H <sub>2</sub> -producing bacteria; ( <i>Prevotellaceae</i> , certain groups within the Firmicutes and Archaea)
Obese cohort [11, 26]	↑ gram-negative microbes ↑ <i>Fusobacterium</i> , <i>Escherichia-Shigella</i> , <i>Pseudomonas</i> and <i>Campylobacter</i>
Obese children and overweight women [30, 41]	↑ <i>Staphylococcus aureus</i>
Obese cohort on preoperative diet [42]	↓ <i>Streptococcaceae</i> and <i>Ruminococcaceae</i> ↑ <i>Rikenellaceae</i> and <i>Bifidobacteriaceae</i>
Post-bariatric surgery [37, 42, 43]	↑ Gammaproteobacteria ( <i>Enterobacteriaceae</i> ) ↓ Firmicutes ( <i>Clostridium difficile</i> , <i>Clostridium hiranonis</i> , and <i>Gemella sanguinis</i> ) ↓ methanogens
Post-bariatric surgery [43, 44]	↑ <i>Escherichia</i> , <i>Klebsiella</i> , and <i>Pseudomonas</i>
Six months post-bariatric surgery [42]	↑ <i>Streptococcaceae</i> and <i>Veillonellaceae</i> ↓ <i>Bifidobacteriaceae</i>
Rodent model – post bariatric surgery [45]	↑ Bacteroidetes, Verrucomicrobia, and Proteobacteria ↑ <i>Alistipes</i> , <i>Akkermansia</i> , and <i>Escherichia</i>
Rodent model – post bariatric surgery [46]	↑ Proteobacteria ( <i>Enterobacter hormaechei</i> ) ↓ Firmicutes and Bacteroidetes
Allogenic FMT recipients [47]	↑ <i>Roseburia intestinalis</i>



# JONA Microbiome analysis is complex – Drug response



**Increased in responders:**  
*Bacteroides dorei*, *Lachnospirillum*  
*sp.*, *Roseburia inulinivorans*

**Increased in non-responders:**  
*Butyricimonas virosa*, *Mitsuokella*,  
*Dialister*, *Alistipes*, *Moryella*

**Responders:**  
 ↑ SCFA producers  
 ↓ LPS-induced inflammation  
 ↑ GLP-1 secretion  
 ↑ HbA1c reduction





# The gut microbiome can be modified

Diet



Supplements



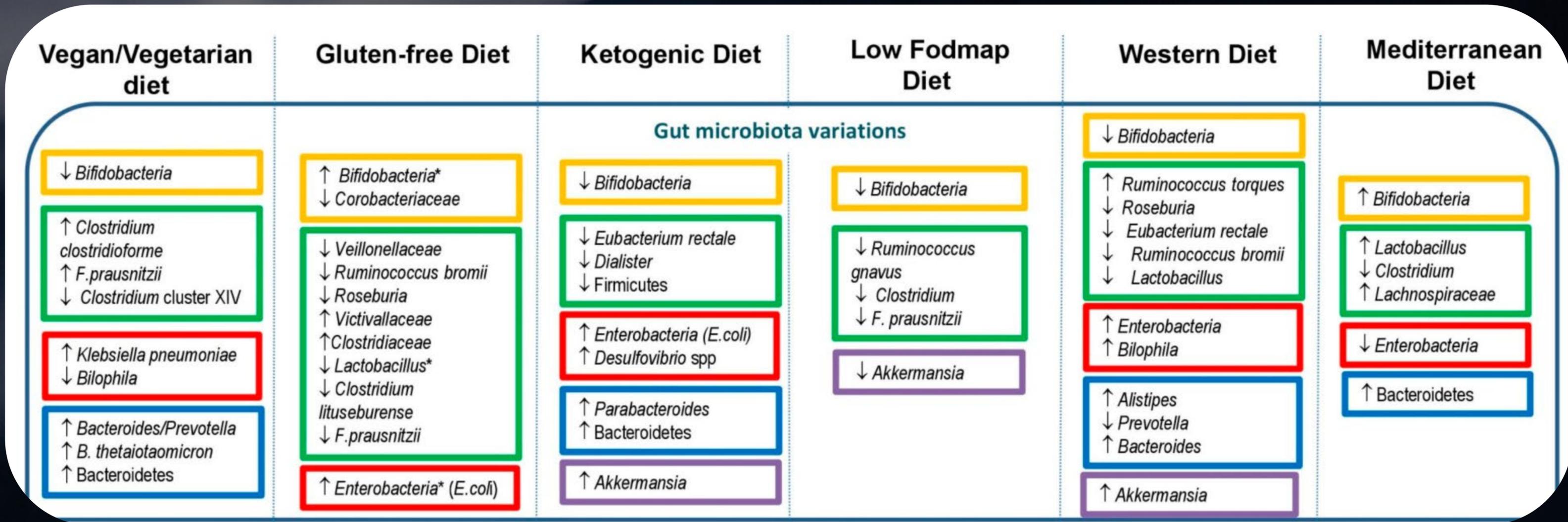
Lifestyle



Medications



# JONA Microbiome change is complex



# JONA Microbiome literature is confusing - Akkermansia

SCIENTIFIC  
REPORTS

nature research

OPEN

## Remission in Crohn's disease is accompanied by alterations in the gut microbiota and mucins production

Daniéla Oliveira Magro<sup>2</sup>, Andrey Santos<sup>1</sup>, Dioze Guadagnini<sup>1</sup>, Flavia Moreira de Godoy<sup>3</sup>, Sílvia Helena Monteiro Silva<sup>1</sup>, Wilson José Fernandes Lemos<sup>4</sup>, Nicola Vitulo<sup>4</sup>, Sandra Torriani<sup>4</sup>, Lilian Vital Pinheiro<sup>2</sup>, Carlos Augusto Real Martinez<sup>2</sup>, Mario José Abdalla Saad<sup>1</sup> & Claudio Saddy Rodrigues Coy<sup>2</sup>

Previous studies have demonstrated that patients with Crohn's disease (CD) in remission do not exhibit an improvement in gut microbiota composition, which might trigger relapses. The present study investigated the dysbiosis and mucins production in CD patients during remission. We performed an analytical cross-sectional single center study, which recruited 18 CD patients and 18 healthy controls (CG) residing in the same home, meaning that all of the participants experienced the same environmental factors, with similar hygiene status, diet, pollution and other common lifestyle characteristics that may influence the composition of the gut microbiota. When compared to healthy controls, the CD patients exhibited lower microbial  $\alpha$ -diversity ( $p = 0.047$ ), a greater abundance of the Proteobacteria phylum ( $p = 0.037$ ) and a reduction in the Deltaproteobacteria class ( $p = 0.0006$ ). There was also a reduction in the *Akkermansia* ( $p = 0.002$ ) and *Oscillospira* ( $p = 0.024$ ) genera and in the proportion of the yeast *Saccharomyces cerevisiae* ( $p = 0.01$ ). Additionally, CD patients in remission presented increased neutral ( $p = 0.001$ ) and acid mucin ( $p = 0.002$ ) concentrations. The reductions in the proportions of *Oscillospira* and *Akkermansia* genera, sulfate-reducing bacteria and *Saccharomyces cerevisiae*, observed in the CD group, may account for the increased mucins production observed in these patients.

Crohn's disease (CD) is characterized by chronic inflammation of the gastrointestinal (GI) tract, and is associated with an increase in the production of inflammatory cytokines, such as interleukins (IL) and tumor necrosis factor alpha (TNF- $\alpha$ ). The disease involves complex interactions among the host immune system, intestinal mucosa and gut microbiota. Interestingly, the gut microbiome has been receiving more attention, and is thought to play a more important role than previously thought<sup>2</sup>. For example, alterations in microbial composition of the intestines, or dysbiosis, and damage to the intestinal mucosal barrier can lead to frequent clinical manifestations, such as diarrhea and weight loss<sup>3,4</sup>. The severity of the intestinal inflammation has been associated with the largest number of colonization sites of gut microbiota with lipopolysaccharide (LPS) endotoxin activity<sup>3-5</sup>.

The colonic mucus barrier is considered the first line of defense against antigens and bacteria present in the intestinal lumen. It is composed of glycoproteins, trefoil factors and mucins<sup>6</sup>. In fact, it was previously reported that changes in the secretion patterns of mucins may be a primary event in CD or secondary to the observed inflammation<sup>7</sup>. Two types of mucins produced by the GI tract include, neutral and acid. In the upper GI tract, neutral mucins are predominantly secreted, while acid mucins prevail in the colon<sup>5</sup>. Additionally, studies have demonstrated that mucins content and expression are important for modulating short chain fatty acid (SCFA) synthesis, affecting the anti-inflammatory and immunological roles of these compounds<sup>3,4</sup>. Despite the apparent

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The relative abundance of *Deltaproteobacteria* class was high in CG group compared with CD (CG  $1.23\% \pm 0.33$  vs CD  $0.4\% \pm 0.21$ ;  $p = 0.0006$  unpaired test and  $p = 0.007$  paired test) (Fig. 4C). In addition, there was reduction of the beneficial genera *Akkermansia* (CG  $0.68\% \pm 0.27$  vs CD  $0.04\% \pm 0.02$ ;  $p = 0.002$  unpaired test and  $p = 0.005$  paired test) (Fig. 4D) and *Oscillospira* (CG  $1.20\% \pm 0.33$  vs CD  $0.55\% \pm 0.15$ ;  $p = 0.024$  unpaired test and  $p = 0.025$  paired test) (Fig. 4E) when compared to CG<sup>19</sup>. Although the analysis of the gut microbiota in this study showed

## Akkermansia is good! Too little Akkermansia is linked with Crohn's Disease (Inflammatory Bowel Disease)



# JONA Microbiome literature is confusing - Akkermansia



## HHS Public Access

Author manuscript

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Mov Disord. 2017 May ; 32(5): 739–749. doi:10.1002/mds.26942.

### Parkinson's Disease and PD Medications Have Distinct Signatures of the Gut Microbiome

Erin M. Hill-Burns, PhD<sup>1</sup>, Justine W. Debelius, PhD<sup>2</sup>, James T. Morton, BS<sup>3</sup>, William T. Wissemann, BA<sup>1</sup>, Matthew R. Lewis, MS<sup>1</sup>, Zachary D. Wallen, MS<sup>1</sup>, Shyamal D. Peddada, PhD<sup>4</sup>, Stewart A. Factor, DO<sup>5</sup>, Eric Molho, MD<sup>6</sup>, Cyrus P. Zabetian, MD, MS<sup>7</sup>, Rob Knight, PhD<sup>2,3,8</sup>, and Haydeh Payami, PhD<sup>1,9,\*</sup>

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#### Data accession

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of Medicine of University of Alabama at Birmingham.

in study-specific differences such as the populations that were studied. Our results (Table S3 E) confirmed many of the reported associations including elevated levels of *Akkermansia*,<sup>12</sup> *Lactobacillus*,<sup>13</sup> and *Bifidobacterium*<sup>14</sup> and reduced levels of *Lachnospiraceae*<sup>12</sup> in PD. We did not, however, replicate the reported association with *Prevotellaceae*<sup>11</sup> (case vs. control P=0.57, association with UPDRS III score P=0.24).

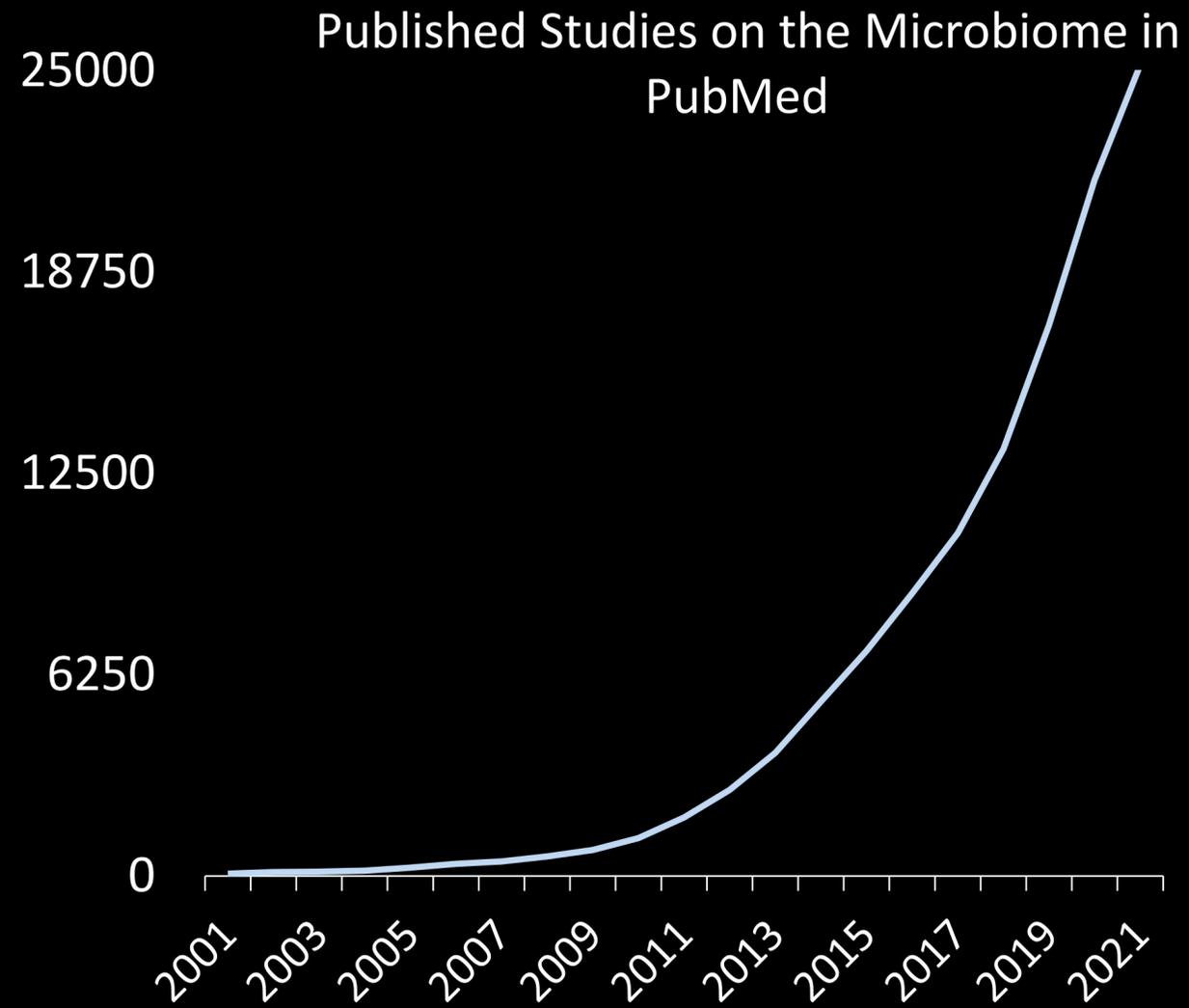
....Akkermansia is bad?

Too much Akkermansia is linked with Parkinson's Disease



# JONA

## Microbiome literature exploding



>2000 papers per month is more than anyone can possibly read

Jona built a custom AI to read literature and interpret a microbiome test



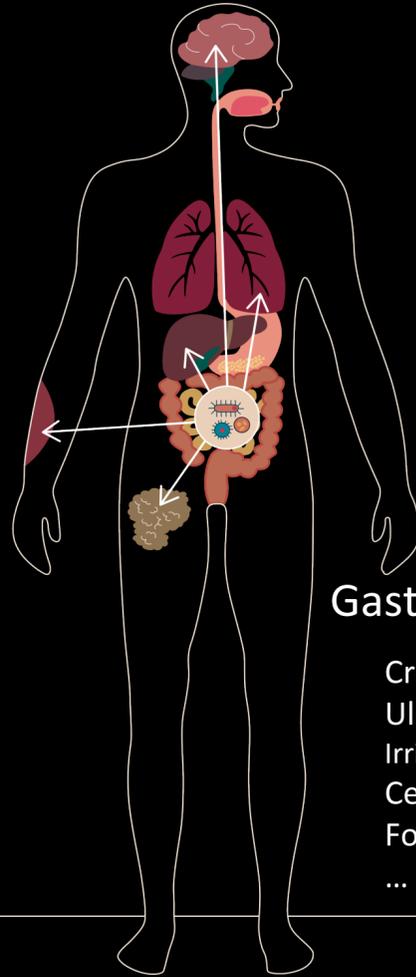
# Jona assesses linked conditions and the effect of interventions

Compare patient microbiome to every study in the literature

Create virtual post-intervention microbiota from literature

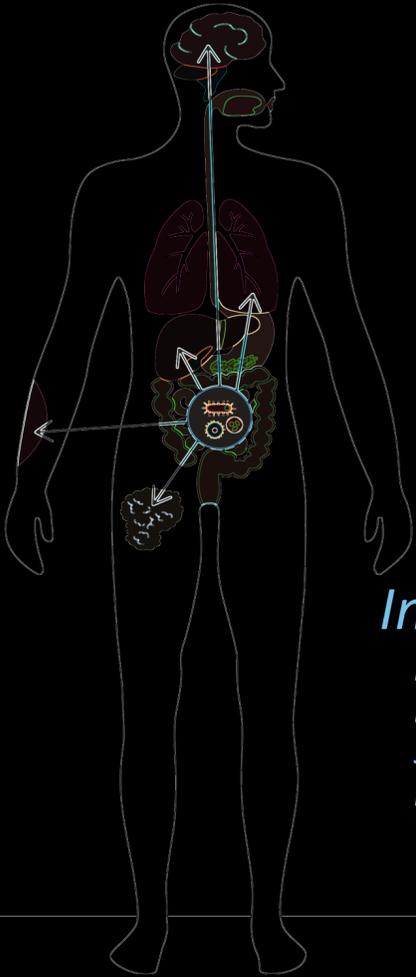
Compare each virtual patient microbiome post-intervention to all profiles in the literature

Recommend interventions that lower associations and avoidance of interventions that increase associations



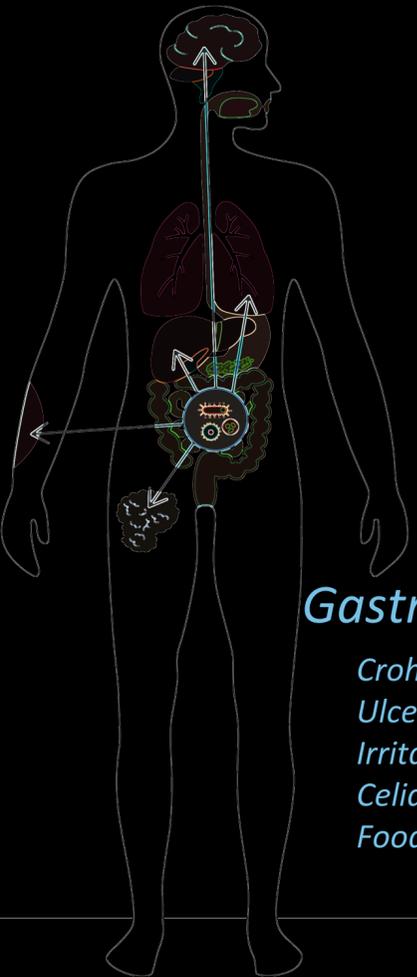
## Gastro-intestinal

- Crohn's disease
- Ulcerative colitis
- Irritable bowel syndrome
- Celiac
- Food allergy
- ...



## Interventions

- Diet
- Lifestyle
- Supplements
- Medications



## Gastro-intestinal

- Crohn's disease
- Ulcerative colitis
- Irritable bowel syndrome
- Celiac
- Food allergy

Jona provides next generation microbiome analysis

### Here is your action plan:

#### 1. Removing trigger foods can alleviate weight gain

Lactose is a natural sugar found in milk and dairy products. It is a disaccharide composed of glucose and galactose. Some individuals have lactose intolerance, a condition in which they lack the enzyme needed to digest lactose properly, leading to digestive discomfort. Foods that naturally contain lactose include milks (from cow, sheep, or goat), yogurt, kefir, ice cream, and butter. Lactose can also be found in some processed foods.

#### 2. Consider the following diet changes to improve weight gain

Resistant starch (RS) is a type of starch known for its resistance to digestion in the digestive tract, undergoing fermentation by gut microbes. This unique property can aid in blood sugar regulation. Examples of foods containing RS include legumes (like lentils and barley), tubers (including potatoes and yams, particularly when cooled after cooking and then cooled, such as sushi rice). Additionally, specific breads and green banana flour also provide sources of resistant starch.

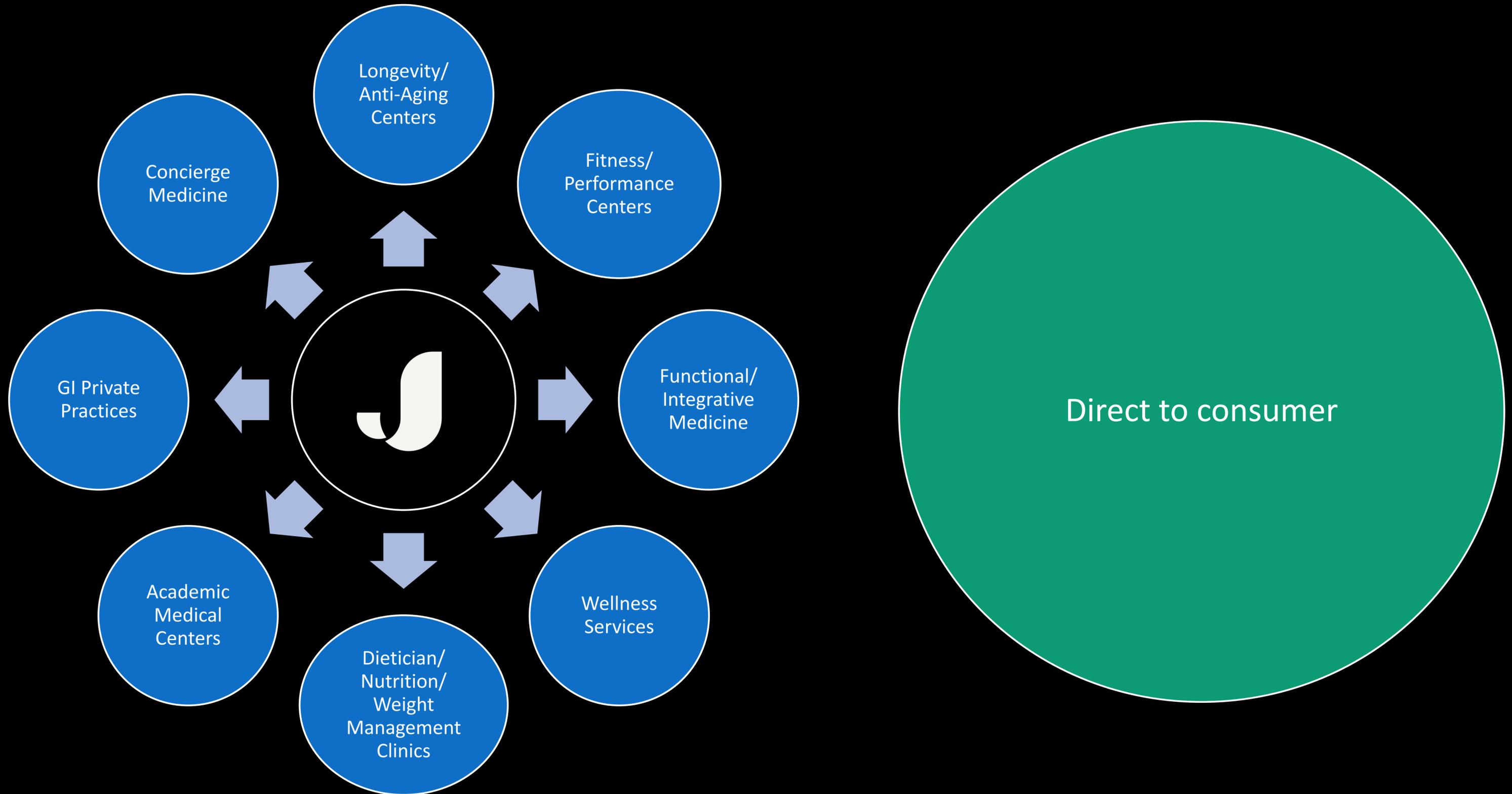
#### Impact on microbiome

#### 3. Speak to your doctor if you are concerned about any of the fo

Crohn's disease is a type of inflammatory bowel disease (IBD) that causes inflammation in the digestive tract, from the mouth to the anus. Common symptoms of Crohn's Disease include abdominal pain, diarrhea, and weight loss. Crohn's disease is associated with gut microbiome dysbiosis. Research shows that certain bacterial groups, such as increased adherent-invasive Escherichia coli (AIEC) and reduced levels of other beneficial groups, are found in individuals with Crohn's disease. Changes in the gut microbiome can disrupt the barrier function of the intestinal walls, which may worsen or trigger inflammation.

#### Highest impact actions

# Cash pay – Both providers and direct to consumer



# JONA

## Questions?

Contact to Partner with Jona

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